Pharmacologie médicale

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Drug usage patterns of Pylera® in France using the national claims reimbursement database

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Abstract

Background: Pylera®, a capsule-based therapy with bismuth, metronidazole, and tetracycline, is prescribed for eradication of Helicobacter pylori (*H. pylori*). Due to the history of bismuth encephalopathy risk, the French Health Authority requested a post-marketing program in France including a drug utilization study.
Objectives: To describe the usage patterns of Pylera® in a real-life setting.
Methods: Cohort study of patients with a 1st dispensing of Pylera® between April 2013 and April 2014, identified in a representative national French reimbursement database, the *Echantillon Généraliste des Bénéficiaires* (EGB), which is a 1/97th sample of the nationwide French claims and hospitalisation database (66 million persons, SNIIRAM). Patients had a 12-month clinical history and follow-up from the index date. Misuse (main criterion) was defined as a dispensing of more than one pack of Pylera® at index date or a dispensing not preceded by diagnostic test in 12-month before 1st dispensing.
Results: 540 patients with a first dispensing of Pylera® were included. Their main characteristics were: mean age of 53 years, 44% of men and 18% previously treated for the eradication of *H. pylori* in 12-month before index date. The main prescribers were gastroenterologists or hospital physicians (61%), followed by general practitioners (30%). A proton pump inhibitor was co-dispensed for 93% of patients, mainly omeprazole (65%) and esomeprazole (17%). 9 patients (2%) had a hepatic or renal impairment, and one patient was pregnant. 59 patients (11%) met the misuse criterion: 10 had more than one pack of Pylera® (7 patients with 2 packs, 2 with 3 packs, and one with 4 packs), and 49 without urea breath test or endoscopy before index date. Taking also into account the serology test as a diagnostic test, the misuse criterion decreased to 51 patients (9%). Within the 1-year follow-up period, 45 patients (8%) had a new tritherapy prescription to eradicate *H. pylori*.
Conclusions: This real-life nationwide French claims and hospitalisation database study showed a misuse of Pylera® for just over 10% and mostly were misusers because of lack of diagnostic test before Pylera® treatment, and two or more packs of Pylera® dispensed for 2%. Some contraindications were also observed such as hepatic or renal impairment, and pregnancy. A new dispensing of a specific treatment, indication of treatment failure was given to 8% that is close to an eradication failure rate of *H. pylori* infection in France between 10% and 30% as shown in the literature.

Conflict of Interest Statement

This study was performed at the request of the French Health Authorities, supported by an unconditional grant from successively Axcan, Forest, Actavis, Aptalis, Allergan, and supervised by an independent expert Scientific Committee. It was designed, conducted, and analyzed independently by the Bordeaux PharmacoEpi Platform, CIC Bordeaux CIC1401 of the Bordeaux University. This study was registered with the European Medicine agency's EUPAS registry (www.encepp.eu), under study number EUPAS3901, and carries the "ENCePP Study" seal.

Background

- **Pylera®:** capsule-based therapy with bismuth, metronidazole, and tetracycline, indicated in eradication of Helicobacter pylori (*H. pylori*).
- **MAA** in France 10 April 2013.
- **Bismuth (Bi) withdrawn from French market** in 1975 for an **encephalopathy risk**.
- Due to this potential risk, the French Health Authority has requested to conduct a post-marketing program in France including **a drug utilization study.**

Objectives

- **Principal objective:** To evaluate the misuse of Pylera® in France.
- **Secondary objectives:**
  - ✓ To describe the characteristics of Pylera® users,
  - ✓ To describe the new prescription of specific treatment to eradicate *H. pylori*.

Method

- **Cohort study** of patients with a 1st dispensing of Pylera® between April 2013 and April 2014 (index date) and 12 month of follow-up.
- **Data source: the *Echantillon Généraliste des Bénéficiaires* (EGB)**, which is a permanent and representative 1/97th sample of the nationwide French claims and hospitalisation database (66 million persons, *Système National d'Information Inter-Régimes de l'Assurance Maladie* - SNIIRAM).
- **12-month data history** from the index date.
- **Misuse (main criterion):** dispensing of more than one pack of Pylera® at index date or dispensing not preceded by diagnostic test in 12-month before 1st dispensing.
- Descriptive statistical analyses and confidence intervals at 95% (CI 95%) with Clopper-Pearson method.

Results

- **Analysis population**

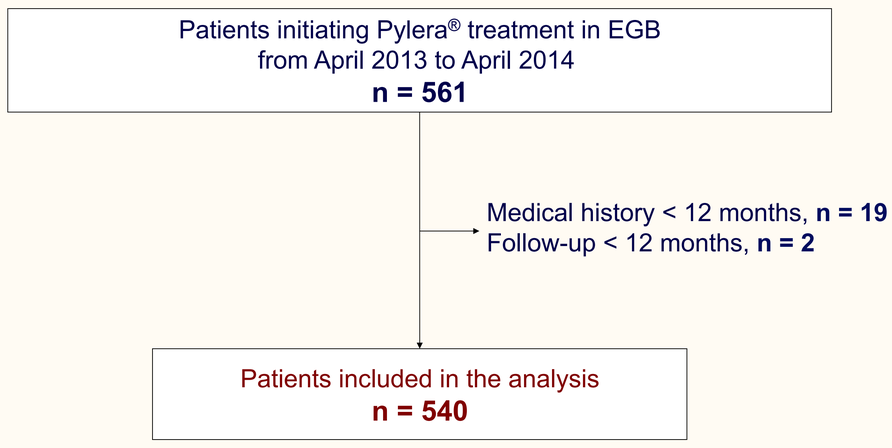

Figure 1: Identification and selection of patients for data analysis

- **Characteristics of the Pylera® population**
  - ✓ Patients characteristics of the 540 patients identified in the EGB with a first dispensing of Pylera® between April 2013 and April 2014 are described in Table 1.

Table 1: Patients characteristics of the Pylera® population

	Pylera® population n = 540	
Men, n (%)	240	(44.4)
Age at index date (in years)		
Mean (± SD)	53.0	(15.5)
[Min ; Max]	[14.0; 93.0]	
Age at index date (in categories), n (%)		
< 12 years	-	
[12 - 18[years	3	(0.6)
[18 - 90[years	536	(99.2)
≥ 90 years	1	(0.2)
Pregnant or nursing women, n (%)	1	(0.2)
Patients with abnormal liver or renal function, n (%)	9	(1.7)
At least one LTD[1] declared or ongoing (in the 12 months before index date), n (%)	161	(29.8)
Type 1 diabetes and type 2 diabetes	59	(10.9)
Malignant tumours, malignant lymphatic or hematopoietic tissue	44	(8.1)
Long-term psychiatric conditions	22	(4.1)
Severe arterial hypertension	17	(3.1)
Severe heart failure arrhythmias valvular cardiomyopathy congenital cardiomyopathy	16	(3.0)
Coronary heart disease	15	(2.8)
Chronic obstructive pulmonary disease (COPD)	10	(1.9)
Unlisted LTD	8	(1.5)
At least one dispensing of specific tritherapy to eradicate *H. pylori* (in the 12 months before index date), n (%)	8.0	(3.3)
At least one UBT[2] or endoscopy (in the 12 months before index date), n (%)	491	(90.9)
At least one UBT, serology test or endoscopy (in the 12 months before index date), n (%)	499	(92.4)
At least one co-dispensing of PPI at index date, n (%)	504	(96.0)
Omeprazole	342	(65.1)
Esomeprazole	89	(17.0)
Pantoprazole	49	(9.3)
Rabeprazole	25	(4.8)
Lansoprazole	14	(2.7)
Medical specialty of Pylera® prescribers at index date, n (%)		
Gastroenterology and hepatology	243	(45.0)
General practitioner	160	(29.6)
Hospital physician (undetermined specialty)	84	(15.6)
Surgery	4	(0.7)
Unknown or other specialty	49	(9.1)

[1]LTD: Long-Term Disease; [2] UBT: Urea Breath Test; [3]PPI: Proton Pump Inhibitor

- **Conditions of Pylera® use**
  - ✓ At index date, 59 patients (11%) met the misuse criterion, the majority of which (83%) for lack of UBT or endoscopy within the 12 months before index date.
  - ✓ Tacking into account the serology test as a diagnostic test, the number of patients with misuse criterion decreased from 59 to 51 (9%) (Table 2).

Table 2: Normal use and misuse of Pylera® at index date

	Pylera® population n = 540		95 % CI[1]
Normal use, n (%)	481	(89.1)	[86.4; 91.7]
Misuse, n (%)	59	(10.9)	[8.3; 13.6]
Dispensing of more than one pack of Pylera® at index date, n (%)	10	(1.9)	-
2 packs	7	(1.3)	
3 packs	2	(0.4)	
4 packs	1	(0.2)	
No UBT, serology test and/or endoscopy performed during the 12 months preceding index date, n (%)	49	(9.1)	-
Normal use (tacking into account serology), n (%)	489	(90.6)	[88.1; 93.0]
Misuse (tacking into account serology), n (%)	51	(9.4)	[7.0; 11.9]
Dispensing of more than one pack of Pylera® at index date, n (%)	10	(1.9)	-
No UBT, serology test and/or endoscopy performed during the 12 months preceding index date, n (%)	41	(7.6)	-

[1] Clopper-Pearson Binomial Exact 95 % CI

- **New dispensing of specific treatment to eradicate *H. pylori***
  - ✓ A new dispensing of Pylera® or another specific treatment to eradicate *H. pylori* in the 12 months after the first dispensing of Pylera® (treatment failure indicator) was observed for 45 patients (8%).
  - ✓ More than a third of them (17 out of 45) had a new dispensing in the 3 months after the first dispensing of Pylera® (Table 3).

Table 3: New dispensing of specific treatment to eradicate H. pylori within 12-month of follow-up

	New dispensing to eradicate *H. pylori*		95 CI[1]
During treatment period	3	(0.6)	[0.1; 1.6]
10 days after treatment period	3	(0.6)	[0.1 ; 1.6]
1 month after treatment period	6	(1.1)	[0.4 ; 2.4]
3 months after treatment period	17	(3.1)	[1.7 ; 4.6]
1 year after treatment period	45	(8.3)	[6.0 ; 10.7]

[1] Clopper-Pearson Binomial Exact 95 % CI

Conclusion

- According to nationwide French claims and hospitalisation database, misuse of Pylera® concerned 10% of patients, mainly due to a lack of diagnostic test before Pylera® treatment.
- 2% of patients had some contraindications such as hepatic or renal impairment, and pregnancy.
- 8% of patients had a new dispensing of a specific treatment, indicator of treatment failure that is close to in the literature with an eradication failure rate of *H. pylori* infection in France between 10% and 30%.